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EXAMINER

LEITH, PATRICIA A

ART UNIT

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/749,602	Applicant(s) EMERY ET AL.	
	Examiner Patricia Leith	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 10 October 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 34-44, 67-69, 71-82, and 84-102 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34-44, 67-69, 71-82, and 84-102 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

. DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/10/2008 has been entered.

Claims 34-44, 67-69, 71-82, and 84 –102 remain pending in the application and were examined on their merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34, 37, 39-43, 67-69, 83-86, 89, 91-95 and 97-102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766) in view of Genovese et al. (1998) in light of Sharma et al. (US 4458630 A)* for the reasons of record.

Claims 34-44, 67-69, 71-82, and 84 –102 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766) and further in view of Evans et al. (US 6,500,438 B2) in view of Genovese et al. (1998) in light of Sharma et al. (US 4458630 A)*.

Applicants have newly amended their independent claims; i.e., claims 34, 69 and 84 to include the limitation of "...capable of mounting an adaptive immune response

to the immunogen.” While this term is not explicitly used in Applicants disclosure, it is determined to be implied because the crux of Applicants’ invention is to vaccinate birds in-ovo. Vaccination is inherently an adaptive immune response, in that vaccination prompts an immune response comprising the production of antibodies specific for the antigen they are being vaccinated against. Similarly, because the prior art makes clear that the birds are being *vaccinated in-ovo*, this inherently would include mounting an adaptive immunity

Applicants’ arguments were fully considered, but not found to be persuasive.

Applicants initially argue that the prior art does not explicitly teach wherein the inoculated eggs comprise maternal antibodies to the siderophore receptor as required by the claimed invention (pp. 11-13, Remarks). The Examiner has already acquiesced to this assertion by Applicants. However, the prior art none-the-less implicitly provides motivation to do so as keenly described in the previous Office actions. “[a] person of ordinary skill is also a person of ordinary creativity, not an automaton *KSR* 127S. Ct. at 1742.

To reiterate from the previous Office action, one of ordinary skill in the art would have had a reasonable expectation that inoculation of the egg with a siderophore receptor protein would have had a reasonable expectation of success, even though

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maternal antibodies toward the siderophore receptor protein were present in the egg.

Applicant has not convincingly demonstrated that an immune response *will not be* elicited in an egg which has circulating maternal antibodies. Because Emery et al. was directed toward inoculation of an egg, one of ordinary skill in the art; for example, one who raises chickens for produce, would be motivated to inoculate all of the eggs of each successive generation of bird (or chicken or another avian species) according to well-known guidelines set forth in the prior art; i.e., Phelps et al. and Evans et al.. This flows naturally from the combined teachings of the prior art. Thus, once an egg has been inoculated it will more than likely have some maternal antibodies to the inoculated antigen. Regardless of the fact that the egg would or would not contain maternal antibodies toward the antigen, the ordinary artisan would have been motivated to further inoculate the eggs produced by this chicken which had been inoculated *in-ovo* because there would be a reasonable expectation that the inoculation would have afforded the unhatched bird *some immunity to the antigen*. Further, although the claims state that a maternal antibody must be present, there is no indication as to what amount the maternal antibodies must be present, and therefore, the claims could be directed toward as little as one antibody present in the egg. This is due to the fact that it is a guess as to when the vaccines should be given since *there is no verifiable means given in the Instant specification in order to quantify the antibody titers of the fertilized eggs, or to predict the amount of maternal antibodies in a given avian egg or to predict the maternal antibody titers in a hatched chick*. Therefore, the Instant specification gives preferred protocols of when to inoculate the eggs, assuming that the maternal antibody titers are

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'reduced' in the egg. However, this concept is deemed obvious because the prior art references clearly taught that the claimed times for inoculation of an avian as well as the particular protocol parameters found in the claims were well-known.

Applicants tend to assert that because the prior art did not explicitly teach inoculation of eggs of chickens previously inoculated when they were embryos, that the claims are patentable over the prior art. However, the Examiner respectfully disagrees. It is clear from the prior art as a whole that egg inoculation would continue amongst generations of poultry. Inoculation of an egg with a siderophore receptor present in a chicken previously inoculated when it was an embryo with the same siderophore receptor would necessarily contain maternal antibodies to the siderophore receptor. This is an obvious method implied by the prior art and is not considered to be the patentable crux of the claimed invention. It would have been well-within the skill of the ordinary artisan at the time the invention was made to inoculate eggs from chickens over and over again, in order to afford newly hatched poults immunity to siderophore receptors of gram negative bacteria in order to produce healthy broods in successive generations of poultry.

Applicants argue that Genovese et al. teach potentiating an innate immune response...Genovese et al. did not teach 'inoculating' birds at 4-7 days, as suggested in the Office action, because 'inoculating' requires administration of an

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antigen or disease causing agent..." (p. 14, Remarks). However, the crux of the Genovese et al. publication is to vaccinate young poult against bacterial infection; namely, *Salmonella enteritidis*. Applicants are directed toward p. 3 wherein day old turkey poult were challenged with SE (*Salmonella enteritidis*). Vaccination with a foreign antigen will necessarily produce an innate as well as adaptive immune response. Genovese et al. clearly teaches that immunization within the first few days of hatching is beneficial because, to reiterate, Genovese et al. states "... it would be advantageous to administer an agent which could potentiate an immediate immune response for protection during the 4 to 7 days when the birds are most susceptible to these bacterial invaders and vaccination responses have not yet taken full effect". Genovese et al. further state in the same paragraph that "poultry have been shown to be most susceptible to bacterial species such as *Salmonella* during the first 4 days of life". Further, Genovese et al. state that "vaccinations currently used on newly hatched chicks and poult do provide some levels of protection"(emphasis added).

Applicants argues that innate and adaptive immune responses are different and that Genovese et al. are solely concerned with potentiating an innate response and not with inducing an adaptive immune response and cites Genovese et al: "...it would be advantageous to administer an agent which could potentiate an immediate immune response for protection during the 4 to 7 days when the birds are most susceptible to these bacterial invaders and vaccination responses have not yet

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taken full effect"...Whereby Applicants state: "This statement refers to potentiating an innate immune response to compensate for the lack of an adaptive immune response to antigens as a result of vaccination with bacterial antigens". However, clearly, a vaccination has already been given to the poults in the time required by the claimed invention. Thus, although Genovese et al. stimulate the immune systems of the bird post-vaccination, the vaccinations have none-the-less been administered during the time as required by the claimed invention. Hence, the teachings of Genovese et al. to advantageously stimulate the immune system in general, does not obviate the fact that their ultimate goal is to provide immunization to young poultry against Salmonella. Furthermore, the claimed invention merely requires that the bird is *capable* of mounting an adaptive immune response to the immunogen. Thus, the claims are broad enough to read on wherein the bird is capable of producing *one antibody* to the antigen administered to the egg. There is nowhere in the claims that requires that the egg is in fact immune toward the siderophore receptor. Applicant has not provided any clear evidence that inoculation with SE (Genovese et al.) or inoculation with siderophore receptors of gram negative bacteria (Emery et al.) would not be capable of mounting an adaptive immune response; on the contrary, Genovese et al. clearly taught that "vaccinations currently used on newly hatched chicks and poults do provide some levels of protection" (p. 5). Although they also do teach "...the typical humoral/cell-mediated immune response requires 7 to 10 days to reach protective levels..." this does not teach away from the claimed invention because Genovese et al. are merely

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indicating that the antibody titers in the poultts are not very protective levels until 7 to 10 days: but this does not mean that the vaccinations *do not produce antibodies*.

The ordinary artisan, reading the above-cited reference would clearly understand that vaccination of poultts with SE on day one would induce antibodies against SE, even if the antibodies were not in protective amounts. Again, the claims do not require total immune protection, the claims only require that the chicks are 'capable of producing an adaptive immune response.' Judging from the teachings of the prior art, from day one poultts are capable of mounting an adaptive immune response.

Further, to reiterate from the previous Office action, the claims are broad enough to include any time period wherein the maternal antibodies are 'reduced' which is a very broad term, tending to be directed toward any time after hatching, or wherein the implant provides for a sustained or delayed release for a certain period of time such as 1-90 days or 1-60 days or 1-35 days as stated in the dependant claims. Clearly, *these times were within the preferred times of vaccination as taught by Genovese et al.* Again, the term 'reduced' in the claim is very broad and it is deemed that the times of inoculation as disclosed by Genovese et al. fit the description of 'reduced' maternal antibodies in light of the Instant specification, the Instant claims and especially absent evidence to the contrary.

Additionally, Applicants are reminded that the 'sustained' and 'delayed' release of the immunogen as related by the claimed invention takes place between 1-90, 1-60 or 1-35 days post-hatching. While Applicants tend to stress that this is a crucial period for immunization, it is plainly clear that the prior art already taught as such and thus, the times as Instantly claimed for delivering a siderophore receptor are not deemed inventive; on the contrary, the combined teachings of the prior art provide a clear roadmap to the claimed invention. The claimed invention is thus predictable and one of ordinary skill in the art would have had a reasonable expectation of success based upon the combined teachings of the prior art.

Applicants argue that because it was known in the prior art that the presence of maternal antibodies posed a competing threat to newly vaccinated birds, that one of ordinary skill in the art would not be motivated to inoculate an egg which possessed maternal antibodies to the antigen one wished to introduce into the egg: "One skilled in the art would not have been motivated to vaccinate eggs laid from subsequent-and, presumably, non-naïve-generation precisely because one skilled in the art understood that the presence of the maternal antibodies against the immunogen would interfere with induction of an adaptive immune response..." (pp. 16-17, Remarks). However, this is in direct contradiction to Genovese et al. who teach immunization at one day of hatching. While it may have been recognized that maternal antibodies may interfere with a chick producing an immune response, immunizations were none-the-less given in day old poults. Again, the claims are

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merely directed toward providing a sustained release until the bird is capable of mounting an immune response, wherein this time is limited by the claims as being within 1-90 days post-hatching (for example, see claim 39). Seeing that Genovese et al. already determined that antibodies are produced in day-old turkey poults, one of ordinary skill in the art would have had a good expectation that delaying a sustained release formulation containing siderophore receptor as disclosed by Emery et al. to release one day after hatching would have produced at least one antibody in a chick thereby fulfilling the requirements of the claimed invention.

Applicants argue that “Sharma et al. suggest...using cell-associated delivery of a virus – an approach inappropriate for delivery of SRPs- and Genovese et al. induced an innate immune response. Moreover, the suggested combination fails to provide one skilled in the art with a reasonable expectation that inoculating eggs with an immunogen would provide a protective adaptive immune response...” (p. 18, Remarks). However, Applicants are arguing limitations which are not found in the claimed invention; namely 'a protective adaptive immune response.' It is reminded that the claims only require that the '*bird is **capable** of mounting an immune response*' which is made obvious by combination of the prior art documents.

. The teachings of Sharma et al. while indicating that an immune response may be elicited *in-ovo* do not verifiably teach away from the claimed invention, especially

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in light of the combination of the references which specifically teach the advantageous nature of immunizing a hatched bird squarely within the time frames as claimed by Applicants. Again, while Applicants as well as the prior art recognize that there is a point in time after the hatching of a bird that maternal antibodies decrease, thereby providing an advantageous window where an exceptional immune response can be elicited in a bird, *Applicants have not disclosed such a window, as such a window would vary from bird to bird.* While Applicants have provided data in the Instant specification which gives a rough estimate of when the maternal antibodies have decreased, claim 34 for example recites "wherein the implant provides for sustained release of the immunogen until the maternal antibodies in a bird hatching from the egg *are reduced so that the bird is capable* of mounting an immune response." First, no data has been provided which quantitates maternal antibody titers present *in an egg or in a hatched bird.* Again, the term 'reduced' is very broad, and it is not quite understood what this means. It is thus deemed that in light of the combined teachings of the prior art, that if an embryo *is capable of enabling an immunogenic response to an antigen, then the maternal antibodies must have been 'reduced' enough in order for the embryo to be 'capable of' mounting an immune response to the immunogen.* Similarly, even though it was not the preferred embodiment of Genovese et al. , this reference clearly taught that immune responses were possible within 1-4 days of hatching. This also follows from *Applicants' own claims which state that the immunogen is released from 1-n days*

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(where n=90 or 60 or 35). Thus, Applicants' arguments tend to contradict their own claimed invention.

Claims 34, 37, 39-43, 67-69, 83-86, 89, 91-95 and 97-102 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,538,733) in view of Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766).

Emery et al. (US 5,538,733) discussed the problem of vaccination of young animals in that maternal antibodies present in neonates may interfere with an animal's immune response, while proposing a solution of administration of vaccines present in sustained and delayed delivery agents to young poultry between the ages of 1-90 days (see entire reference and Abstract). Emery et al. explicitly indicated that the method advantageously incorporated injection of an 'implant matrix' made of "...biocompatible, biodegradable, bioabsorbable and/or bioerodible polymeric material.." such as cholesterol and cellulosic polymers to "...release the immunogen for sustained delivery into surrounding tissue fluids over an about 1-90 day period" (see, col. 2, lines 15-55).

Emery et al. specifically indicated that "The continuous presence of a priming dose of the immunogen provides an effective way of priming a young animal so that a secondary immune response to a pathogenic infection is stimulated

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substantially immediately when passive protection by maternal antibodies *against the pathogen* is no longer effective" (see paragraph bridging columns 3-4, emphasis added). Hence, it is clear that Emery et al. is stating that the immunized poultry possess the maternal antibodies against the same immunogen used to inoculate the animals including domestic fowl (see also col. 9, lines 41-49).

Emery et al. indicated that the 'time-delayed implant' "...will substantially maintain integrity of the matrix for a desired length of time. Preferably, the matrix will remain intact for up to about 3 weeks, or after the level of maternal antibody has significantly declined, at which time the antigen is released from the matrix." (emphasis added) Hence, the matrix is formulated for delayed delivery. Emery et al. further indicate that the matrix is formulated for delayed and sustained delivery: "The matrix may optionally be formulated to include a soluble or insoluble pore-forming agent that will dissipate from the matrix into surrounding tissue fluids causing the formation of pores and/or channels throughout the implant matrix....sodium chloride...carboxymethylcellulose" (see col. 9, lines 29-39).

A preferred immunogen for implantation disclosed by Emery et al. was siderophore receptor protein (SRP) from gram negative bacteria (see col. 7, line 50-col. 8, line 24). See also Example 2, wherein a sustained/delayed release formulation of SRP is administered to 1 day old turkey poults to establish immunity

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against the SRP indicative of an adaptive immune response. Notably, in this Example, Emery et al. specifically indicate that a further preference for delivery time to is between 1-60 days of age.

Emery et al. additionally taught the advantageous nature of administration of a booster "...to stimulate a secondary immune response in the animal," wherein the booster was an SRP. Emery et al. gave a specific example wherein a 21 day implant administered to a turkey poult is given a booster injection after the expiration of the implant, stated by Emery et al. to be 21 days after implantation, at about 28-48 days to stimulate the immune response (see col. 11, lines 1-19). This booster time disclosed by Emery et al. falls completely within the claimed booster time of 3-12 weeks (equates to 21-84 days). Serological profiles to quantify antibody titers to SRP were known at the time of Emery et al. and specifically discussed (see col. 11, lines 33-58).

Emery et al. did not specifically teach wherein the siderophore receptor was administered *in-ovo* at 'a time when maternal antibodies of the bird to the immunogen are sufficiently reduced'. Nor did Emery et al. teach the specific injection times as found in claims 39-42 and 44 or wherein a second dose of immunogen was given at 3-12 weeks post-hatching (claim 43). Emery et al. further did not teach the incorporation of porins into their vaccine.

Emery et al. (US 5,830,479) disclosed a method for immunizing poultry with a siderophore from gram-negative bacteria wherein the siderophore is enterochelin or siderophore citrate as examples (col.s 1-53, particularly col. 5, lines 29-38 and claims 1 and 3). As stated by Emery et al. "The vaccine of the present invention may be used for preventing and eliminating infections of gram-negative bacteria in poultry and other animals including humans" (col. 11, lines 9-12). Emery et al. specifically suggested sustained release administration of the vaccine (col. 11, line 15) and *in-ovo* administration in poultry: "The vaccine of the present invention may be used for preventing and eliminating infections of gram-negative bacteria in poultry and other animals, including humans....may be delivered to the animal, for example, by...egg inoculation (i.e., poultry...by known techniques in the art...the vaccine contains an amount of a siderophore receptor protein to stimulate a level of active immunity in the animal to inhibit and/or eliminate gram-negative bacterial pathogenesis and/or sepsis" (col. 11, lines 10-21). Emery et al. specifically taught that "The protein may also be incorporated into a carrier which is a [sic] biocompatible and can incorporate the protein and provide for its controlled release or delivery, for example, a sustained release polymer such as a hydrogel, acrylate, polylactide, polycaprolactone, polyglycolide or copolymer thereof...an example of a solid matrix for implantation into the animal and sustained release of the protein antigen into the body is a matabolizable matrix, as described...in US ...4,452,775 (Kent)" (col. 11, lines 27-36). Emery et al. also taught

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the advantageous use of a booster vaccine given “21-28 days after the first injection” and the use of adjuvants such as porins from gram negative bacteria for administration along with SRP’s (see, col. 7, line 50-col. 8, line 9). Emery et al. offered that the amount of vaccine was varied in order to achieve optimal vaccination (see col. 11, line 49- col. 12, line 6).

Phelps et al. (US 5, 339,766) disclosed a method for introducing material into poultry eggs during early embryonic development which included injection of a therapeutic substance contained within a biodegradable matrix such as polylactide polymers (lactides/glycolides) directly into the developing bird egg. Materials intended for delivery included “vaccines, vitamins, antibiotics hormones, enzyme inhibitors, peptides, cells, DNA and other therapeutic molecules” (col. 3, lines 33-36). Phelps et al. discussed that, “Eggs treated by the method of the present invention are preferably fertile eggs which may be in any period of incubation, from early to late... “ (col. 4, lines 15-18). Phelps et al. further explained that “Such beneficial effects included increased growth, disease resistance due to in ovo vaccination, increased percentage hatch of multiple incubated eggs, and otherwise improved physical characteristics of hatched poultry” (col. 1, lines 20-24).

One of ordinary skill in the art would have been motivated to administer a sustained-release formulation *in ovo*, to a bird (i.e., poultry such as chicken) wherein the

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formulation comprised a siderophore receptor such as enterochelin, and wherein the sustained-release formulation was sustained until the hatching of the bird (i.e., 1-60 or 1-90 days post-hatching) in order to increase the bird's immune system to foreign disease causing bacteria. It was clear from the prior art that siderophore receptors from gram-negative bacteria were known to vaccinate birds, and suggested for use *in-ovo* by Emery et al. '479. Further disclosed by Emery et al. as well as Phelps et al. were suitable mediums and sustained release biocompatible matrices for *in-ovo* injection of vaccines. The ordinary artisan would have recognized, in view of Emery '773 that sustained release of SRPs to young poultry or poultry embryos (in-ovo) would need to be formulated to release the SRPs at a time that the immunogen is "sufficiently reduced so that the birds are capable of mounting an adaptive immune response". This knowledge in the art of poultry immunization is made perfectly clear by Emery '773 and is not considered a novel idea. It is clear from the teachings of the references as a whole, that the Emery et al. patent '773 although not teaching egg inoculation of their sustained/delayed release matrix SRP vaccine is cured by the subsequent Emery '479 patent which clearly suggests that the same matrix, including SRP and advantageously the addition of porin as an adjuvant, into an egg to vaccinate young poultry.

In-ovo vaccination techniques as claimed were known and well-utilized and rendered obvious at the time the Invention was made as evidenced by Phelps et al. Emery et al. '773 and Emery et al. '749 together taught optimal times for vaccinating young poultry at a time when maternal antibodies were reduced in order for the bird to

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mount an immune response; Emery et al. '773 teaching specifically times advantageous to administer such a vaccine which included SRP when maternal antibodies to SRP were 'sufficiently reduced': the 'time-delayed implant' "...will substantially maintain integrity of the matrix for a desired length of time. Preferably, the matrix will remain intact for up to about 3 weeks, or after the level of maternal antibody has significantly declined, at which time the antigen is released from the matrix." It is the opinion of the Examiner that at the time the invention was made, the claimed invention was well-within the purview of the ordinary artisan. Time delayed/sustained matrices for delivering SRP to poultry were known in the art at the time the invention was made and known to be manipulated to release SRP at a desired time. Clearly, the results achieved by both Emery et al. patents include successful vaccination of young poult anywhere from injection at one day (with the sustained delivery matrix of Emery et al. '773), three weeks (see Example 3, Emery et al. '479), six weeks (Emery et al. '479).

Clearly, there is no explicit time indicated in the prior art nor the Instant specification of 'until the maternal antibodies in a bird hatching from the egg are reduced so that the bird is capable of mounting an adaptive immune response to the immunogen' because this time would vary from bird to bird. Hence the reason for the delayed/sustained release formulations of both Emery et al. patents. Such a formulation intended for sustained/delayed release would provide continual vaccine delivery over a desired amount of time in order to successfully vaccinate young birds.

Claims 34-44, 67-69, 71-82, and 84 –102 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Emery et al. (US 5,830,479) in view of Phelps et al. (US 5, 339,766) in view of Emery et al. (US 5,538,733).and further in view of Evans et al. (US 6,500,438 B2).

The teachings of Emery et al. '749, Emery et al. '773 and Phelps '776, were discussed *supra*. None of these references specifically taught t the specific injection protocols as recited in claims 35, 36, 38 and 44.

Evans et al. (US 6,500,438 B2) taught a method for *in ovo* vaccination of chickens with *E. sporozoites* via injection, wherein the injection was preferentially performed in the final quarter of incubation or specifically at day 18 of incubation, however would have been effective during any time of incubation (col. 2, lines 1-6, col. 3 lines 25-27 and Example 1).

Hence, although the prior art did not teach a specific embodiment where SRP was injected into bird eggs at the claimed injection times as required by claims 35, 36, 38 and 44, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A. It is clear from the prior art teachings as a whole that the sustained

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release matrices including SRP and advantageously including porins as an adjuvant to the SRP vaccine were formulated to release during a time that maternal antibodies to the vaccine were sufficiently reduced in order for the chick to produce antibodies to the vaccine. Such matrices were well-known in the art and producing such compositions was within the skill level of the ordinary artisan at the time the invention was made. In-ovo injections to produce an immune response were further known in the prior art to be carried out within the time frames specified by the claims. There is no one limitation within the claims which is deemed to be directed toward a novel invention; as the prior art provides a clear roadmap to the claimed invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia Leith whose telephone number is (571) 272-0968. The examiner can normally be reached on Monday - Friday 8:30am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on (571) 272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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